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Prehospital Antibiotic Administration for Suspected Open Fractures: Joint COT/OTA/ACEP/NAEMSP/NAEMT Position Statement

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Abstract

One of the primary concerns associated with open fractures is the development of a fracture-related infection (FRI). To minimize the risk of developing an FRI and subsequent morbidity, prophylactic antibiotics should be administered to patients with open fractures as soon as possible. While the antibiotic recommendations for severe open fractures are somewhat debatable, the use of a cephalosporin remains a mainstay of prophylactic treatment. Though administration of prehospital antibiotics does represent an expansion of EMS responsibilities, there have been several other treatment expansions in the prehospital setting, such as the administration of tranexamic acid and the application of pelvic binders. The administration of antibiotics, specifically cefazolin, is inexpensive, technically simple, and does not require special storage. The following recommendations are supported by and represent consensus of the COT, OTA, ACEP, NAEMSP and NAEMT with regards to prehospital antibiotic prophylaxis for suspected fractures:

1. In a responsive patient with no history of penicillin or cephalosporin allergy, the administration by EMS of a 1st generation cephalosporin should be performed after the management of life threats. This intervention should not delay transport.

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2. In an obtunded patient, the administration by EMS of a 1st generation cephalosporin should be performed after the management of life-threats. This intervention should not delay transport.
 3. In a responsive patient with a documented penicillin allergy, the administration by EMS of a 1st generation cephalosporin should be performed with close monitoring after the management of life-threats. This intervention should not delay transport.
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Introduction

Open fractures involve any broken bone with an associated open wound that allows for communication with the external environment. These injuries are often the result of high-energy trauma (e.g., motor vehicle crashes, falls from height, pedestrians struck) but can also be seen in lower-energy environments, such as falls from standing in the elderly population. They can be suspected in the field when a fractured bone is visible, there is a large wound over an obvious deformity, or with a partial or complete amputation. Gustilo and Anderson originally described open fractures based on the size of the open wound and the degree of soft tissue disruption in tibia fractures (1). Type one fractures have a wound one centimeter or less, the wound in type two fractures is slightly larger but less than ten centimeters, and type III wounds are ten centimeters or greater and sometimes necessitate vascular repair or flap coverage (1).

One of the primary concerns associated with these injuries is the development of a fracture-related infection (FRI) (2). Open fractures are at high risk for FRI given their direct communication with the environment, the associated soft tissue injuries, and contamination at the time of injury (1). Additionally, FRI are often the cause of significant orthopedic complications, such as osteomyelitis (infection of the bone) and non-unions, both of which represent a substantial cost to both society and the patient. To minimize the risk of developing an FRI and subsequent morbidity, prophylactic antibiotics should be administered to patients with open fractures as soon as possible (1, 3, 4). Significant research has been performed to determine the appropriate pharmacologic interventions for these injuries, as well as to delineate the importance of timing associated with antibiotic prophylaxis (1, 4, 5). The need for rapid administration of antibiotics in these injuries makes early administration a key intervention that can be provided in the prehospital setting to improve patient outcomes. The American College of Surgeons Committee on Trauma (COT), the Orthopedic Trauma Association (OTA), the American College of Emergency Physicians (ACEP), the National Association of EMS Physicians (NAEMSP), and the National Association of Emergency Medical Technicians (NAEMT) drafted the recommendations below after review of the evidence and expert consensus.

History of Antibiotics in Open Fracture Prophylaxis

Historically, it was thought that time to operative debridement was the key predictor of outcomes in open fractures; however, multiple studies have subsequently demonstrated that this is not the driving factor in reducing infectious complications (6, 7). More importantly, the use of antibiotics in open fractures has been common orthopedic practice for over four decades and has been shown to decrease the rate of FRI (1, 4). These studies demonstrate

that antibiotic prophylaxis is one of the most important interventions in preventing infectious complications associated with open fractures.

Importance of Time to Antibiotics

Multiple studies have examined the role of the timing of delivery of antibiotics to infectious outcomes associated with open fractures. A study by Lack et al., demonstrated a significant increase in infectious complications when antibiotic prophylaxis was delayed 66+ minutes past the time of injury (8). Several clinical studies have demonstrated that quality improvement processes can decrease the time of hospital delivery of antibiotics to closer to this 66-minute threshold (9-12). While these studies are retrospective in nature and thus have associated limitations, they represent the best data available on the impact of early antibiotic prophylaxis on open fractures. Additionally, the 2006 Surgical Infection Society and the Eastern Association for the Surgery of Trauma (EAST) Practice Management Guidelines recommend that antibiotic prophylaxis be delivered to open fracture patients as soon as possible, further reiterating the importance of timeliness to prevent infectious complications associated with open fractures (13, 14). Even with this knowledge, timely administration of antibiotics for open fractures remains challenging, and many centers report delays in antibiotic administration (15, 16). One study performed in 2019 queried the National Trauma Data Bank and demonstrated that the average across all centers of patients receiving antibiotics within 1 h of arrival was 47.6% (15).

Prolonged extrication and transportation times can delay the administration of antibiotics since they are typically given upon reaching the hospital. This is key for patients injured in rural settings, where multiple studies have demonstrated that EMS response and transport times are often much longer than their urban counterparts (17, 18). Given the greater geographical distances covered in the rural areas, it is likely that there is a corresponding increase in time to antibiotics administration for these patients due to prolonged travel times. In many cases, these transport times exceed an hour from the time of injury, already putting patients outside of the ideal administration window (8, 18).

Role of EMS

Several studies have evaluated the efficacy and safety of antibiotic administration to patients with open fractures by EMS clinicians (19-22). These studies demonstrate a low inappropriate administration rate and a strong safety profile for antibiotic administration (19-21). Additionally, these studies also show a decreased time to antibiotic administration than if they waited until arriving at the emergency department (19, 20). In the study by Hendrickson et al., they were able to decrease time to administration by 20 min (from 180 min to 160 min on average), but likely because this was still substantially longer than the previously described window of opportunity, they could not find a decrease in complications. Collopy et al., reported zero allergic reactions when a cephalosporin was administered prior to arrival at a hospital in their cohort of 278 patients (21). In this manner, EMS can play a critical role in the care of open-fracture patients and reduce the risks of negative sequelae associated with open fractures (21). EMS clinicians can help improve patient outcomes and decrease the societal burden of infections in open fracture patients (23).

While the administration of prehospital antibiotics does represent an expansion of EMS responsibilities, there have been several other treatment expansions in the prehospital setting, such as the administration of tranexamic acid and the application of pelvic binders (24-27). The administration of antibiotics, specifically cefazolin, is inexpensive, technically simple, and does not require special storage. The greatest costs associated with the use of antibiotics for suspected open fractures are associated with personnel training, monitoring of supplies and replacement of expired medications. While these are not insignificant, they are in line with previous expansions of EMS care and the benefits of this intervention are vast. The greatest technical challenge for this is the establishment of IV access. These examples support the feasibility of expanding the prehospital phase of care, which can be done in a safe and productive manner.

Antibiotic administration in the field should never be done prior to the management of immediate life threats of the patient and should not delay transport. Prehospital antibiotic administration in most systems would be best done during the transport phase after stabilization of the patient.

Antibiotic Selection

The use of cephalosporin in the prophylactic treatment of open fractures is well supported in the literature and by several surgical societies. In 2006, the Surgical Infection Society published guidelines supporting the use of a short course of a first-generation cephalosporin as prophylactic treatment for open fractures (13). This recommendation was reiterated in the 2022 update to the Surgical Infection Society guidelines (28). Both the 2006 and 2022 guidelines stated that further data is needed to recommend for or against the use of gram-negative prophylaxis (13, 28). The EAST Practice Management Guidelines similarly recommend gram-positive coverage of all open fractures (14). In various unique clinical scenarios, different antibiotic recommendations have been made. In barnyard injuries, adding Penicillin G has been recommended as further prophylaxis against clostridium species (14). In fractures occurring in bodies of water or in combat theaters, fluoroquinolones have been recommended as an adjunct therapy for extended gram negative coverage and prophylaxis against aquatic pathogens (e.g., *vibrio* and *aeromonas* species) (29).

In much of the orthopedic literature, certain antibiotics are recommended to cover gram-negative bacteria in high-grade open fractures. However, strong evidence to support this prophylaxis is lacking (3, 5). The EAST Practice Management Guidelines do endorse (at a lower evidence-based recommendation) the use of aminoglycosides for grade II and grade III open fractures, though evidence for this is limited (14). However, many of the antibiotics recommended for gram-negative coverage can have serious systemic side effects (e.g., nephrotoxicity and ototoxicity), and thus, the risk-benefit ratio should be considered (30). While the antibiotic recommendations for severe open fractures are somewhat debatable, *the use of a cephalosporin still remains a mainstay of prophylactic treatment* (15).

The choice of cefazolin 2 g intravenous in the prehospital setting is designed to be safe and rapid and cover potential gram-positive bacteria in suspected open fractures. Additionally, a one-time dose of cefazolin for suspected open fractures would be in line with most, if

not all, antimicrobial stewardship guidelines. Given the limitation of requiring IV access in the field, ideally, there would be an IM or oral option. However, currently, there is no data to support this alternative. Antibiotic decisions to expand coverage can be made based on hospital protocols once the patient arrives in the emergency department.

Cefazolin Safety and Cross-Reactivity

Cefazolin allergy is rare, and the few reported side effects are generally mild. Anaphylactic reactions, while serious events are fortunately very uncommon with cefazolin. This safety profile has led to it becoming one of the most widely used antibiotics in orthopedic procedural settings (31). In most centers, the first dose of cephalosporin is given as 2 grams, even in patients with renal impairment. Historically, the rate of penicillin allergy having cross-reactivity with a cephalosporin was reported to be as high as 10%. However, these claims have not been validated and have, in fact, been refuted by newer studies (32, 33). Additionally, it was also discovered that in many of these initial reports, there was a high rate of contamination of the cephalosporins with penicillin; this likely caused the rate of reported cross-reactivity to be falsely high (31). Newer level one data, in adult and pediatric populations, has demonstrated that this rate of cross-reactivity of cefazolin with penicillin is lower than 1%, and administering cefazolin to penicillin-allergic patients is very safe (34, 35). We therefore recommend that in the obtunded patient where allergies are unknown, cephalosporins are safe with appropriate monitoring.

Pediatric Treatment

While there has been some debate regarding the need for surgical debridement of pediatric open fractures, there is a consensus that antibiotic prophylaxis should be provided to these patients (36, 37). While these recommendations are based largely on adult studies, the recommendation for rapid gram-positive coverage for pediatric populations is still consistent across the orthopedic literature (36, 37). The largest drawbacks to antibiotic use in the field for pediatrics are with regards to weight-based dosing and being able to obtain IV access. However, in children under 50kg 1 g of Cefazolin has been accepted dosing and in children over 50kg 2 g is the accepted dosage, hopefully minimizing this concern.

COT/OTA/ACEP/NAEMSP/NAEMT Recommendations

The above organizations support the following recommendations for patients with suspected open fractures for EMS clinicians whose scope of practice allows for the administration of antibiotics and whose agencies have the resources to administer prehospital antibiotics.

1. In a responsive patient with no history of penicillin or cephalosporin allergy, the administration by EMS of a 1st generation cephalosporin should be performed after the management of life threats. This intervention should not delay transport.
2. In an obtunded patient, the administration by EMS of a 1st generation cephalosporin should be performed after the management of life-threats. This intervention should not delay transport.
3. In a responsive patient with a documented penicillin allergy, the administration by EMS of a 1st generation cephalosporin should be performed with close

monitoring after the management of life-threats. This intervention should not delay transport.

Conclusion

Open fractures represent a common injury with the potential for serious infectious-related sequelae along with significant patient and societal costs. Early antibiotic prophylaxis plays a critical role in the prevention of infection. The early administration of a 1st generation cephalosporin has been shown to decrease the rate of infections in open fractures. Additionally, this medicine has an excellent safety profile in patients with and without a penicillin allergy. Through early antibiotic administration in the prehospital setting, EMS clinicians can play a crucial role in the treatment of these patients in preventing serious long-term infectious sequelae. As with all prehospital interventions, this implementation should be part of the system approach, and coordination with the receiving facility is essential. We recommend early, pre-hospital administration of prophylactic antibiotics for open fractures while not delaying transport to the receiving hospital or superseding any normal life or limb-saving care provided in the field.

References

1. Gustilo RB, Anderson JT. Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective analyses. *J Bone Joint Surg Am*. 1976;58(4):453–458. doi:10.2106/00004623-197658040-00004. [PubMed: 773941]
2. Metsemakers WJ, Morgenstern M, McNally MA, Moriarty TF, McFadyen I, Scarborough M, Athanasou NA, Ochsner PE, Kuehl R, Raschke M, et al. Fracture-related infection: a consensus on definition from an international expert group. *Injury*. 2018;49(3):505–510. doi:10.1016/j.injury.2017.08.040. [PubMed: 28867644]
3. Gustilo RB, Mendoza RM, Williams DN. Problems in the management of type III (severe) open fractures: a new classification of type III open fractures. *J Trauma*. 1984;24(8):742–746. doi:10.1097/00005373-198408000-00009. [PubMed: 6471139]
4. Patzakis MJ, Harvey JP, Ivler D. The role of antibiotics in the management of open fractures. *J Bone Joint Surg Am*. 1974;56(3):532–541. doi:10.2106/00004623-197456030-00010. [PubMed: 4150798]
5. Wilkins J, Patzakis M. Choice and duration of antibiotics in open fractures. *Orthop Clin North Am*. 1991;22(3):433–437. doi: 10.1016/S0030-5898(20)31673-4. [PubMed: 1852421]
6. Weber D, Dulai SK, Bergman J, Buckley R, Beaupre LA. Time to initial operative treatment following open fracture does not impact development of deep infection: a prospective cohort study of 736 subjects. *J Orthop Trauma*. 2014;28(11):613–619. doi:10.1097/BOT.0000000000000197. [PubMed: 25050748]
7. Schenker ML, Yannascoli S, Baldwin KD, Ahn J, Mehta S. Does timing to operative debridement affect infectious complications in open long-bone fractures? A systematic review. *J Bone Joint Surg Am*. 2012;94(12):1057–1064. doi:10.2106/JBJS.K.00582. [PubMed: 22572980]
8. Lack WD, Karunakar MA, Angerame MR, Seymour RB, Sims S, Kellam JF, Bosse MJ. Type III open tibia fractures: immediate antibiotic prophylaxis minimizes infection. *J Orthop Trauma*. 2015;29(1):1–6. doi:10.1097/BOT.0000000000000262. [PubMed: 25526095]
9. Johnson JP, Goodman AD, Haag AM, Hayda RA. Decreased time to antibiotic prophylaxis for open fractures at a level one trauma center. *J Orthop Trauma*. 2017;31(11):596–599. doi:10.1097/BOT.0000000000000928. [PubMed: 29053543]
10. Goodman AD, Modest JM, Johnson JP, Hayda RA. A simple initiative to decrease time to antibiotic prophylaxis for open fractures is durable after 2 years. *J Am Acad Orthop Surg*. 2021;29(18):e932–e939. doi:10.5435/JAAOS-D-20-00075. [PubMed: 33399289]

11. Harvey S, Brad Hall A, Wilson K. Impact of an emergency medicine pharmacist on initial antibiotic prophylaxis for open fractures in trauma patients. *Am J Emerg Med.* 2018;36(2):290–293. doi:10.1016/j.ajem.2017.10.039. [PubMed: 29079370]
12. Collinge CA, McWilliam-Ross K, Kelly KC, Dombroski D. Substantial improvement in prophylactic antibiotic administration for open fracture patients: results of a performance improvement program. *J Orthop Trauma.* 2014;28(11):620–625. doi:10.1097/BOT.0000000000000090. [PubMed: 24662993]
13. Hauser CJ, Adams CA, Eachempati SR. Surgical infection society guideline: prophylactic antibiotic use in open fractures: an evidence-based guideline. *Surg Infect.* 2006;7(4):379–405. doi:10.1089/sur.2006.7.379.
14. Hoff WS, Bonadies JA, Cachecho R, Dorlac WC. East practice management guidelines work group: update to practice management guidelines for prophylactic antibiotic use in open fractures. *J Trauma.* 2011;70(3):751–754. doi:10.1097/TA.0b013e31820930e5. [PubMed: 21610369]
15. Barnard ER, Stwalley D, Miller AN. State of the Union: timeliness to antibiotics in open fractures. *J Orthop Trauma.* 2023; 37(5):e213–e218. doi:10.1097/BOT.0000000000002546. [PubMed: 36729516]
16. Lin CA, O'Hara NN, Sprague S, O'Toole RV, Joshi M, Harris AD, Warner SJ, Johal H, Natoli RM, Hagen JE, et al. Low adherence to recommended guidelines for open fracture antibiotic prophylaxis. *J Bone Joint Surg Am.* 2021;103(7):609–617. doi:10.2106/JBJS.20.01229. [PubMed: 33411466]
17. Grossman DC, Kim A, Macdonald SC, Klein P, Copass MK, Maier RV. Urban-rural differences in prehospital care of major trauma. *J Trauma.* 1997;42(4):723–729. doi:10.1097/00005373-199704000-00024. [PubMed: 9137264]
18. Jones MD, Paulus JA, Jacobs JV, Bogert JN, Chapple KM, Soe-Lin H, Weinberg JA. Trauma patient transport times unchanged despite trauma center proliferation: a 10-year review. *J Trauma Acute Care Surg.* 2021;90(3):421–425. doi:10.1097/TA.0000000000003049. [PubMed: 33306601]
19. Lack W, Seymour R, Bickers A, Studnek J, Karunakar M. Prehospital antibiotic prophylaxis for open fractures: practicality and safety. *Prehosp Emerg Care.* 2019;23(3):385–388. doi:10.1080/10903127.2018.1514089. [PubMed: 30141716]
20. Winstanley RJH, Hadfield JN, Walker R, Bretherton CP, Ashwood N, Allison K, Trompeter A, Eardley WGP. The open-fracture patient evaluation nationwide (OPEN) study: the management of open fracture care in the UK. *Bone Joint J.* 2022;104-B(9):1073–1080. doi:10.1302/0301-620X.104B9.BJJ-2022-0202.R1. [PubMed: 36047016]
21. Collopy K, Zimmerman L, Westmoreland AM, Powers W. Prehospital administration of cefazolin in trauma patients. *Air Med J.* 2022;41(5):447–450. doi:10.1016/j.amj.2022.06.001. [PubMed: 36153141]
22. Hendrickson SA, Donovan R, Harries L, Wright TC, Whitehouse MR, Khan U. Time to intravenous antibiotic administration (TibIA) in severe open tibial fractures: impact of change to national guidance. *Injury.* 2020;51(4):1086–1090. doi:10.1016/j.injury.2020.03.005. [PubMed: 32164953]
23. Iliaens J, Onsea J, Hoekstra H, Nijs S, Peetermans WE, Metsemakers WJ. Fracture-related infection in long bone fractures: a comprehensive analysis of the economic impact and influence on quality of life. *Injury.* 2021;52(11):3344–3349. doi: 10.1016/j.injury.2021.08.023. [PubMed: 34474918]
24. Fischer PE, Bulger EM, Perina DG, Delbridge TR, Gestring ML, Fallat ME, Shatz DV, Doucet J, Levy M, Stuke L, et al. Guidance document for the prehospital use of tranexamic acid in injured patients. *Prehosp Emerg Care.* 2016;20(5):557–559. doi:10.3109/10903127.2016.1142628. [PubMed: 26985786]
25. Almuwallad A, Cole E, Ross J, Perkins Z, Davenport R. The impact of prehospital TXA on mortality among bleeding trauma patients: a systematic review and meta-analysis. *J Trauma Acute Care Surg.* 2021;90(5):901–907. doi:10.1097/TA.0000000000003120. [PubMed: 33605702]
26. Bangura A, Burke CE, Enobun B, O'Hara NN, Gary JL, Floccare D, Chizmar T, Pollak AN, Slobogean GP. Are pelvic binders an effective prehospital intervention? *Prehosp Emerg Care.* 2023; 27(1):24–30. doi:10.1080/10903127.2021.2015024. [PubMed: 34874811]

27. Schweigkofler U, Wohlrath B, Trentzsch H, Horas K, Hoffmann R, Wincheringer D. Is there any benefit in the pre-hospital application of pelvic binders in patients with suspected pelvic injuries? *Eur J Trauma Emerg Surg.* 2021;47(2):493–498. doi:10.1007/s00068-019-01239-6. [PubMed: 31612271]
28. Buckman SA, Forrester JD, Bessoiff KE, Parli SE, Evans HL, Huston JM. Surgical infection society guidelines: 2022 updated guidelines for antibiotic use in open extremity fractures. *Surg Infect (Larchmt).* 2022;23(9):817–828. doi:10.1089/sur.2022.206. [PubMed: 36350736]
29. Lloyd BA, Murray CK, Shaikh F, Carson ML, Blyth DM, Schnaubelt ER, Whitman TJ, Tribble DR. Early infectious outcomes after addition of fluoroquinolone or aminoglycoside to posttrauma antibiotic prophylaxis in combat-related open fracture injuries. *J Trauma Acute Care Surg.* 2017;83(5):854–861. doi:10.1097/TA.0000000000001609. [PubMed: 28570348]
30. Petejova N, Martinek A, Zadrazil J, Kanova M, Klementa V, Sigutova R, Kacirova I, Hrabovsky V, Svagera Z, Stejskal D. Acute kidney injury in septic patients treated by selected nephrotoxic antibiotic agents-pathophysiology and biomarkers-A review. *Int J Mol Sci.* 2020;21(19):7115. doi:10.3390/ijms21197115. [PubMed: 32993185]
31. Sarfani S, Stone CA, Murphy GA, Richardson DR. Understanding penicillin allergy, cross-reactivity, and antibiotic selection in the preoperative setting. *J Am Acad Orthop Surg.* 2022;30(1):e1–e5. doi:10.5435/JAAOS-D-21-00422. [PubMed: 34669610]
32. Dash CH. Penicillin allergy and the cephalosporins. *J Antimicrob Chemother.* 1975;1(3 Suppl):107–118. doi:10.1093/jac/1.suppl_3.107. [PubMed: 1201975]
33. Petz LD. Immunologic reactions of humans to cephalosporins. *Postgrad Med J.* 1971;47(Suppl):64–69.
34. Belmont AP, Su C, Kwah J. Cephalosporins can be safely administered to patients with verified penicillin allergy. *J Allergy Clin Immunol Pract.* 2023;11(9):2933–2835.e2. doi:10.1016/j.jaip.2023.05.027. [PubMed: 37245737]
35. Beltran RJ, Kako H, Chovanec T, Ramesh A, Bissonnette B, Tobias JD. Penicillin allergy and surgical prophylaxis: cephalosporin cross-reactivity risk in a pediatric tertiary care center. *J Pediatr Surg.* 2015;50(5):856–859. doi:10.1016/j.jpedsurg.2014.10.048. [PubMed: 25783308]
36. Pace JL, Kocher MS, Skaggs DL. Evidence-based review: management of open pediatric fractures. *J Pediatr Orthop.* 2012;32(Suppl 2):S123–S127. doi:10.1097/BPO.0b013e318259f326. [PubMed: 22890450]
37. Trionfo A, Cavanaugh PK, Herman MJ. Pediatric open fractures. *Orthop Clin North Am.* 2016;47(3):565–578. doi:10.1016/j.ocl.2016.02.003. [PubMed: 27241379]